

REMARKS

Applicants submit this Amendment in response to the Office Action mailed August 27, 2002. Claims 1-37 are pending in the application. Claims 10-13 and 15-37 have been withdrawn from consideration as being directed to a non-elected invention. Therefore, claims 1-9 and 14 are currently being examined. The specific grounds of rejection are addressed below.

As a preliminary matter, prior to addressing the grounds of rejection, applicants strenuously disagree with the Examiner's assertion (paragraphs 14-16 at pages 8 and 9 of the Office Action) of "new grounds of rejection" without withdrawing the finality of this Office Action. The specific rejections and arguments are discussed in this response at pages 6-8 .

Applicants respectfully request that the Examiner withdraw the finality of this Office Action, consider applicants' arguments below at pages 6-8, and if needed, issue another Action addressing these arguments, thereby giving applicants an opportunity to timely respond prior to entry into the after-final phase of prosecution.

Rejections under 35 U.S.C. § 112, Second Paragraph

Claims 1-9 and 14 stand rejected under 35 U.S.C. § 112, second paragraph, as allegedly indefinite. More specifically, the Action asserts that claims 1-3 are indefinite for reciting the term "about." Without acquiescing to the ground of rejection, applicants have amended claims 1, 3 and 14, which no longer recite the term "about."

In view of the above remarks, applicants submit that the grounds of rejection under 35 U.S.C. § 112, second paragraph, have been overcome. Accordingly, withdrawal of these rejections is respectfully requested.

Rejections under 35 U.S.C. § 112, First Paragraph (Enablement)

Claims 1-9 and 14 stand rejected under 35 U.S.C. § 112, first paragraph, for allegedly being non-enabled. In view of the amendment to claims 1, 3 and 14, applicants submit that the ground of rejection may be withdrawn to the extent that it applies to the "about" claim

language. Regarding the 90% identity language, applicants strenuously traverse the rejection on the grounds that it would not require undue experimentation for one of skill in the art to determine if a nucleic acid at least 90% identical to a claimed polynucleotide encodes a polypeptide that shares the biological activity of the polypeptide encoded by the polynucleotide of SEQ ID NO:3. Example 3 of the application discloses that EGFH2 is a secreted protein. mRNA encoding EGFH2 was injected into *Xenopus* oocytes and induced meiotic maturation via germinal vesicle breakdown. One of ordinary skill in the art can construct nucleic acid molecules corresponding to EGFH2 mRNA that is at least 90% identical to a polynucleotide encoding SEQ ID NO:4, or to a polynucleotide of SEQ ID NO:3. These mRNA molecules can be tested in the *Xenopus* oocyte system as described in Example 3 and the biological activity can be determined.

The Examiner states that the specification fails to provide guidance as to the “core structure” of SEQ ID NO:4 that is essential for maintaining the mitogenic activity. Applicants submit that the issue is whether undue experimentation would be required for one of skill in the art to construct or obtain a polynucleotide according to the claims, and to test it for the biological activity. Analysis of the actual structure is not a required element.

To further support the enablement of the claims, applicants submit herewith a Declaration under 37 C.F.R. § 132 by Dr. Judith Abraham, who has expertise and experience in this area of protein chemistry and activity, as evidenced by her current position as Research Director at Chiron Corporation, and her numerous scientific publications in peer-reviewed journals. Dr. Abraham discusses the fact that EGFH2 of the invention is also known as NRG4, and as such is known to signal through an ErbB receptor. (The relationship between EGFH2 and proteins of the NRG family is discussed in the Specification at page 7, lines 3-16.) For NRG4 (EGFH2), the receptor is ErbB4. Several assays are available for determining if a protein falls within the scope of the claims. These assays are described in detail in paragraphs 6, 7, 8 and 9 of the Declaration. In each case, the results of the assay will provide a definite answer to allow one of ordinary skill in the art to determine if a protein falls within the scope of the claims. These routine assays are in some cases referred to in the specification, or are based on methods and reagents disclosed in the specification and/or well-known to those of skill in the art at the time of filing.

In view of the above remarks and Dr. Abraham's declaration, applicants submit that the grounds of rejection under 35 U.S.C. § 112, first paragraph, have been overcome. Withdrawal of this rejection is respectfully requested.

Rejections under 35 U.S.C. § 112, First Paragraph (Written Description)

Claims 1-9 and 14 stand rejected under 35 U.S.C. § 112, first paragraph, for allegedly lacking an adequate written description. The Examiner states that "one of ordinary skill in the art cannot envision all of the nucleic acid and amino acid substitutions encompassed by the breadth of the claims or all of the isolated nucleic acid molecule that encode from about 1 to about 115 of SEQ ID NO:4 or from about 2 to about 115 of SEQ ID NO:4 and having mitogenic activity." (Office Action at page 5, second full paragraph.)

Without acquiescing to the ground of rejection, and to further the prosecution of the application, the term "about" is no longer recited in claims 1, 3 and 14 as amended. Reconsideration and withdrawal of the rejection are respectfully requested.

NEW GROUNDS OF REJECTION

As a preliminary matter, applicants strenuously disagree with the Examiner's assertion of these alleged "new grounds of rejection" without withdrawing the finality of the Office Action. Applicants' position is supported by two points. First, the Examiner notes an apparent indefiniteness regarding the numbering and/or positions of the amino acids in claims 1, 3-9, and 14. The claim language objected to by the Examiner was present in the originally filed claims 1 and 3. The language was added to claim 14 solely to remove dependency from unelected claim 13; that language therefore was also in the application at the time of filing. Thus, the language could have been addressed by the Examiner at an earlier date in prosecution and cannot be construed as a new ground of rejection while at the same time not permitting applicants an opportunity to address the issue prior to the final rejection. Second, the Examiner stated that "mitogenic activity" was a departure from the specification and claims as originally filed. On the contrary, the specification clearly anticipates mitogenic activity in, for example, a

section entitled "Mitogenic Properties," at page 38, line 14, through page 39, line 3. Addition of language relating to the mitogenic properties of the claimed encoded polypeptide simply incorporates material that was in the application at the time of filing.

Under the present USPTO practice, "second or any subsequent actions on the merits shall be final, except where the examiner introduces a new ground of rejection that is neither necessitated by applicants' amendment of the claims nor based on information submitted in an information disclosure statement...." MPEP § 706.07(a). As outlined in the paragraph above and further explained below, the Examiner's introduction of new grounds of rejection was not necessitated by applicants' amendment of the claims nor based on information in an IDS. Accordingly, the Examiner's final rejection is premature and should be withdrawn under MPEP § 706.07(d). Applicants respectfully request that the Examiner withdraw the finality of the Office Action, consider applicants' arguments below, and if needed, issue another Action addressing these arguments, giving applicants an opportunity to timely respond prior to entry into the after-final phase of prosecution. A discussion of the specific new grounds of rejection follows immediately below.

Claims 1, 3-9 and 14 are rejected under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite. The Examiner stated that (A) it was unclear how an amino acid sequence with 1 or 2 amino acids could have mitogenic activity, and (B) it was not clear whether the claims indicate the number of amino acids or the positions of the amino acids. It is clear from the context of the present specification that the language refers to position, and not to the number of amino acids. See, for example, page 13, lines 18-22, which indicates that the fragments consist of amino acids from, for example, "about 9" to "about 45." If the language meant the number of amino acids, it would be so indicated: such as, "consists of 9 amino acids." The alleged indefiniteness as it pertains to an amino acid sequence of 1 or 2 amino acids having mitogenic activity is moot in view of the correct interpretation of the claims language, in which the number "1", "2" etc. refers to position. However, to further the prosecution, applicants have amended claims 1, 3 and 14 to clearly indicate that the language refers to amino acid positions. Reconsideration and withdrawal of this ground of rejection are respectfully requested.

Claims 1, 3-9 and 14 are rejected under 35 U.S.C. § 112, first paragraph, as allegedly containing new matter, on the grounds that the "mitogenic activity" of claims 1, 3 and

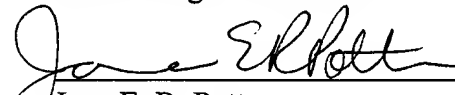
14 represents a departure from the specification and claims as originally filed. Without acquiescing to the ground of rejection, applicants have amended claims 1, 3 and 14 to indicate that mitogenic activity is measured using the *Xenopus* oocyte maturation assay. Regarding claim 3, the Examiner stated that the specification and claims as filed do not provide clear support for the nucleic acid molecule of claim 3 as amended. The mitogenic activity is disclosed at page 38, lines 15-23. The polynucleotides of the invention are disclosed at least at page 2, lines 1-15 and lines 19-26, and page 10, lines 13-24, which describes the biological activity to include mitogenic activity, and further provides that polynucleotides of the invention have equivalent biological activity. Reconsideration and withdrawal of this ground of rejection are respectfully requested.

Attached hereto is a marked-up version of the changes made to the specification and claims by the current amendment. The attached page is captioned **“Version With Markings to Show Changes Made.”**

All of the pending claims in the application are now clearly allowable. Favorable consideration and a Notice of Allowance are earnestly solicited.

Respectfully submitted,

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PATENT TRADEMARK OFFICE

VERSION WITH MARKINGS TO SHOW CHANGES MADE

In the Claims:

Claims 1-3, and 14 have been amended as follows:

1. (Twice amended) An isolated nucleic acid molecule comprising a polynucleotide selected from the group consisting of:

(a) a polynucleotide encoding a polypeptide comprising from [about] amino acid 1 to [about] amino acid 115 of SEQ ID NO:4;

(b) a polynucleotide encoding a polypeptide comprising from [about] amino acid 2 to [about] amino acid 115 of SEQ ID NO:4;

(c) a polynucleotide complement of the polynucleotide of (a) or (b), and

(d) a polynucleotide at least 90% identical to the polynucleotide of (a) or (b) wherein said polynucleotide encodes a polypeptide that has mitogenic activity as determined by *Xenopus* oocyte maturation assay.

3. (Twice amended) An isolated nucleic acid molecule comprising a polynucleotide encoding a polypeptide having an amino acid sequence from [about] amino acid 1 to [about] amino acid 115 or from [about] amino acid 2 to [about] amino acid 115 of SEQ ID NO:4, wherein said polypeptide has at least one conservative amino acid substitution at least 90% identity with SEQ ID NO:4, and mitogenic activity as determined by *Xenopus* oocyte maturation assay.

14. (Twice amended) A composition comprising an isolated polynucleotide encoding a polypeptide comprising an amino acid sequence selected from the group consisting of:

(a) an amino acid sequence from [about] amino acid 4 to [about] amino acid 50 of SEQ ID NO:4;

(b) an amino acid sequence from [about] amino acid 9 to [about] amino acid 45 of SEQ ID NO:4; and

(c) an amino acid sequence at least 86% identical to said amino acid sequence of (a) or (b), wherein said polypeptide has mitogenic activity as determined by *Xenopus* oocyte maturation assay.